

Please add new claim 25 as follows:

Sub C1
B 2

25. (New) A single reagent for the simultaneous determination of total leucocytes, and basophile polymorphonuclear leucocytes, and for the measurement of hemoglobin in a sample of blood, according to claim 12, wherein said nitrogenous compound comprises a quaternary ammonium compound.

REMARKS

Claims 12-24 were pending in the application; claim 13 is hereby cancelled without prejudice as to its readmission by action of the present amendment, and new claim 25 is presented. Claims 12 and 14-25 are now pending; each pending claim defines an invention that is novel and unobvious over the cited art. Favorable consideration of this case is respectfully requested.

Claim 12 is hereby amended to recite a pH lower than 3. Support for this recitation was provided in the original disclosure at, for example, page 4, lines 27-29.

Newly-presented claim 25 recites the nitrogenous compound is a quaternary amine. Support for this recitation was present in the original disclosure at, for example, page 6, lines 16-17.

Claims 1-11 were rejected under 35 U.S.C. § 103(a) as being obvious over U.S. Patent No. 5,677,183 to Tarakada et al. in view of Hamaguchi et al. (5,389,549). To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*. All words in a claim must be considered in judging the patentability of that claim against the prior art. *In re Wilson*. (MPEP § 2143.03). When evaluating the scope of a claim, every limitation in the claim must be considered. See e.g. *In re Ochiai*. (MPEP § 2144.08). The evidentiary record fails to teach each limitation of the present invention.

The present invention, as recited in newly-presented claim 12, comprises a single reagent that permits: (1) the counting of total leucocytes, (2) the differentiation of total leucocytes into the percentage of total leucocytes that is represented by each of the five

Not claimed

leucocyte subclasses, and, (3) the determination of total hemoglobin in a sample of blood. Moreover, as recited in amended claim 12, the single reagent comprises a nitrogenous compound, at least one cationic detergent, the absence of cyanic compounds, and a buffer maintaining the pH at an acidic value less than 3.

First the Examiner specifically acknowledges Takarada to disclose a dual, not a single reagent system. Takarada recites "Thus, leucocytes can be classified into five groups based on the information determined by treating leucocytes with the first reagent and the information determined by treating leucocytes with the second reagent." In addition to failing to achieve the present inventive single reagent, Takarada is silent as to the determination of hemoglobin. Moreover, the Examiner acknowledges that Takarada fails to disclose a nitrogenous compound. Therefore, Takarada fails to meet at least three limitations of the present invention.

Hamaguchi fails to complete Takarada as neither Takarada nor Hamaguchi determine total hemoglobin. Moreover, each of Takarada and Hamaguchi discloses a dual reagent and not the single reagent of the present invention (see Hamaguchi at col. 8, lines 14-18; col. 10, line 45 and col. 11, line 23; col 17, lines 27-30). Therefore, the combination of Takarada and Hamaguchi fails to teach each limitation of the present invention.

The Examiner proposes to complete the teachings of Takarada and Hamaguchi with the teaching of Uchihashi. However, Uchihashi is not properly combinable for the instant purpose because Uchihashi forms inoperable combinations. First, Uchihashi recites "[t]he buffer is not restricted as long as it can maintain a pH at 4.0 to 6.0. Too low a pH makes leucocytes fragile, thereby adversely affecting the measurement of the leucocyte count." (col. 3, lines 49-51). The present invention requires the buffer to maintain a pH value lower than 3. Secondly, The Examiner's combination of Uchihashi with Hamaguchi is improper because Uchihashi and Hamaguchi form an inoperable combination. Hamaguchi recites solutions that do not "employ either saponin or quaternary ammonium compounds." (Abstract). Moreover, Hamaguchi considers "quaternary ammonium salts cause an undesirably high degree of damage to leucocytes." (Col. 5, lines 61-63). Hamaguchi specifically excludes quaternary amines "whereas quaternary ammonium salts are too violent as noted above...neither saponin or quaternary

ammonium salts are used.” (Col 6, lines 34-48). Uchihashi specifically recites quaternary amines “The cationic surfactant preferably includes at least one cationic surfactant of the quaternary ammonium salt type or pyridinium salt type.” (Col. 2, lines 49-51; col. 4, ex. 1-3).

Where the Examiner proposes a combination that makes a prior art reference inoperable for its intended purpose, the resulting inoperable prior art reference is considered to teach away from the proposed combination, thereby supporting a showing of nonobviousness. *In re Gordon*, 733 F.2d 900, 902 (Fed. Cir. 1984) (Finding no suggestion to modify a prior art device where the modification would make the device inoperable for its intended purpose); *TecAir, Inc. v. Denso Mfg. Michigan Inc.*, 192 F.3d 1353, 52 USPQ 2d 1294, 1298 (Fed. Cir. 1999) (Holding that because the combination was inoperable for its intended purpose, a jury could reasonably find the patent taught away from the combination); *In re Sponnoble*, 405 F.2d 578, 587 (CCPA 1969)(Holding if where combined, the references would produce a seemingly inoperative device, the references teach away from their combination).

It is to be further noted that the present invention recites quaternary ammonium compounds as examples of nitrogenous compounds. Hamaguchi specifically excludes quaternary ammonium compounds, and therefore, teaches away from the present invention.

Claims 12-24 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Sakata in view of Hamaguchi and further in view of Uchihashi. The Examiner acknowledges that Sakata fails to teach determination of hemoglobin. Moreover, Sakata fails to distinguish each of the five classes of leucocytes. (See column 6, lines 60-64. Neutrophils are not distinguished from eosinophils; lymphocytes are not distinguished from monocytes). As discussed above, by virtue of the requirement in Hamaguchi that quaternary ammonium compounds be excluded. Hamaguchi and Uchihashi form an inoperable combination. Moreover, for the same reasons, Hamaguchi and the present invention form an inoperable combination. By virtue of forming an inoperable combination, Hamaguchi and Uchihashi cannot be combined to complete any teaching. Sakata also recites reagents containing quaternary ammonium compounds “The cationic surfactant used for the reagent according to the present invention is a quaternary

ammonium salt.” (Col 4, lines 20-22). By virtue of reciting quaternary amines, Sakata and Hamaguchi form an inoperable combination and therefore, per the Federal Circuit, teach away from, and render the present invention non-obvious.

In view of the above, consideration and allowance are, therefore, respectfully solicited.

In the event the Examiner believes an interview might serve to advance the prosecution of this application in any way, the undersigned attorney is available at the telephone number noted below.

The Commissioner is hereby authorized to charge any fees or credit any overpayment associated with this communication, including any extension fees or fees for the net addition of claims, to Deposit Account No. 22-0185.

Respectfully submitted,



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APPENDIX

Please amend claim 12 as follows:

12. (Amended) A single reagent for the simultaneous determination of total leucocytes, and basophile polymorphonuclear leucocytes, and for the measurement of hemoglobin in a sample of blood, said reagent comprising:

a buffer suitable to adjust and maintain the pH to [an acidic value] a value lower than 3;

at least one cationic detergent;

a nitrogenous compound; and further comprising
the absence of cyanic compounds.